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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/373,230	08/12/1999	HARUKI OKMURA	OKAMURA=2E	2359

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/373,230	OKMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-9,11,14 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-9, 11, 14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

The request filed on 01 December 2005 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/373,230 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment filed on 01 December 2005 is acknowledged and entered. Following the amendment, claims 1 and 2 are canceled, and claims 3, 11, 14 and 16 are amended.

Currently, claims 3-9, 11, 14 and 16 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 1 and 2 are moot as the applicant has canceled the claims.

Declaration

A. The rejection of claims 3-6, 11, 14 and 16 based upon lack of enablement (scope) under 35 U.S.C. 112, first paragraph, as set forth in the last Office action is maintained. The declaration of Dr. Haruki Okamura under 37 CFR 1.132 filed 01 December 2005 has been fully considered, but is insufficient to overcome the rejection for the following reasons.

Items 6-9, 13 and 14 of the declaration indicate that Dr. Okamura is one of the inventors who discovered the present IGIF (IL-18) of SEQ ID NO:2; that the skilled person in the art at the time the invention was made could have easily understood and engineered various variants of the protein based on the disclosed amino acid sequence of the IGIF and the biological properties; that the specification does surely enable any person skilled in the art to make the invention commensurate in scope with the claims for variants at least 90% homologous to SEQ ID NO:2. This is not persuasive because the issue is that the disclosed IGIF was a totally new polypeptide not known to belong to any family of proteins, and the specification provide provides no information about the structural and functional relationship of the polypeptide. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural

determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions. However, the present disclosure has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein, which are tolerant to changes, and the nature and extent of changes that can be made in these positions.

B. The prior art rejection of claims 3, 5, 6, 11, 14 and 16 under 35 U.S.C. 102 (b) as anticipated by Nakamura (*Infect. Immun.* 61: 64-70, 1993), set forth in the previous Office actions is maintained. The second declaration of Dr. Haruki Okamura (with the title of "In the European Patent Office") under 37 CFR 1.132 filed 01 December 2005 is insufficient to overcome the rejection for the reasons addressed below under "*Rejections Over Prior Art*", as only item 11 is relevant and it needs to be addressed in context to applicants argument.

New Matter Rejection:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6, 11, 14 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly amended claims 3, 11, 14 and 16 recite "having an amino acid sequence which is at least *90%* homologous to ...", however, while the specification teaches variants having one or more amino acids replaced in SEQ ID NO:2 without

alternating the inherent biological properties of the protein (page 9, for example), it does not provide basis or support for such a specific limitation.

This is a new matter rejection.

Applicants argument filed on 01 December 2005 has been fully considered, but is not deemed persuasive for reasons below.

At pages 10-11 of the response, the applicant argues that while there does not appear to be explicit support for "at least 90% homologous" in the specification as filed, applicants believe that the specification does provide implicit support for such a definition, and that the declaration by Dr. Okamura support such, as it states, in item 10, that "I and other co-inventors had in mind that such variants are those which are at least 90% homologous to ...". This argument is not persuasive because the limitation of "at least 90% homologous" represents a specific scope, which cannot be predicted or anticipated from the general disclosure of the "variants", which can be obtained "by replacing one or more amino acids in SEQ ID NO:2" without altering the inherent biological properties (page 9 of the specification, for example). With respect to the declaration, it does not provide any evidentiary support, and mere something in mind without any specific disclosure cannot be considered as being an inventive concept.

Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6 and 11 remain rejected, and the newly amended claims 14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the previous Office Actions mailed on 05 January 2004, 09 September 2004, and 03 June 2005, and for the reasons below.

Claim 3 remains indefinite for the recitation of "possessing a part or the *whole* of the amino acid sequence of SEQ ID NO:2" in part (4). As the claim is directed to a *variant* of an IGIF (lines 2-3 of the claim), said variant, therefore, cannot possess the whole of the amino acid sequence of SEQ ID NO:2 in the same time. The claim is further indefinite and confusing for

the limitation in the last part of the claim, where it recites that "which is at least 90% homologous to, but different from the amino acid sequence of SEQ ID NO:2". Since "90% homologous to" would automatically mean that the sequence of the variant is different from SEQ ID NO:2, it is redundant to recite "but different from". Claims 11, 14 and 16 are similarly indefinite.

Claim 11 is further indefinite for the recitation of "which *reacts with*" and "or *a variant* ... at least 90% homologous to" in the last part of the claim. It is unclear as to what the term "react with" refers, and whether it means specific binding/recognition. Further, the claim define the structure of the IGIF protein by its interaction with a monoclonal antibody specific to a sequence variant of the protein. Such an antibody may or may not be SEQ ID NO:2 specific, and therefore, it does not help to define the structure of the claimed protein.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6, 11, 14 and 16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to the IGIF of SEQ ID NO:2, and a specific variant of said protein, which has an amino acid sequence of SEQ ID:2 where residue 70 is methionine or threonine, does not reasonably provide enablement for with claims to a variant having physicochemical and functional properties listed in parts (1) to (4) of claim 3, and having the amino acid sequence at least 90% homologous to SEQ ID:2 (claims 3 and 16, for example), reacting with a mAb specific to a variant at least 90% homologous to SEQ ID:2 (claim 11, for example), or a hybridization variant having the amino acid sequence at least 90% homologous to SEQ ID:2 (claim 14, for example), while substantially having the biological activity of (3). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims, for the reasons set forth in the previous Office Actions.

Applicants argument filed on 01 December 2005 has been fully considered, but is not deemed persuasive for reasons below.

At pages 12-14 of the response, the applicant argues that, based on Dr. Okamura's declaration and citing the Watson reference, it would be easy and routine for one of skill in the art to obtain various variants of SEQ ID NO:2 once the amino acid sequence was available at the time the invention was made, and to determine the functional activity of a given variant. This argument is not persuasive for the reasons addressed above, under "Declaration".

Claims 3-6, 11, 14 and 16 remain further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the previous Office Actions.

No argument in response to the instant rejection in the response filed on 01 December 2005.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 5, 6, 11, 14 and 16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper Nos. 4, 7 and 13, and the Office Actions mailed on 09 September 2004, and 03 June 2005.

Applicants argument filed on 01 December 2005 has been fully considered, but is not deemed persuasive for reasons below.

On page 16 of the response, applicants argue that, citing item 11 of the declaration of Dr. Okamura, it is clear that Dr. Okamura (one of the authors of the cited Nakamura reference) did

not consider that the factor disclosed in the Nakamura reference is the same protein as claimed in the present invention, and accordingly, Nakamura does not anticipate the invention. This argument is not persuasive because it is irrelevant as to what Dr. Okamura might have *considered* at the time since the subsequent *evidence* published by Okamura (as addressed in the previous Office Actions) has shown that they are the same molecule. According to MPEP 2124, in certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. *In re Wilson*, 311 F.2d 266, 135 USPQ 442 (CCPA 1962). Such facts include the characteristics and properties of a material or a scientific truism.

With respect to claims 7-9, although the Nakamura does not disclose the sequence of the IGIF, as addressed in the previous Office Action mailed on 7/3/01, the subsequent studies reported by the same group of investigators in the post filling date publications (Okamura et al. (Infection and Immunity, 1995, 63(10):3966-72), and Ushio et al., J Immunol. 156: 4274-4279, 1996) proved that the serum factor initially purified and reported by Nakamura has the same amino acid sequence as that of the present SEQ ID NO:2. As such, the Nakamura reference renders the present claims not novel because, according to MPEP 2112 I., "the court stated that 'just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.'" In the instant case, applicants merely identified the sequence of a protein factor, which had been known and purified in the prior art.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Brenda Brumback
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Dong Jiang, Ph.D.
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AU1646
1/12/06